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THE CONDITION OF THE BLOOD IN CHLOROSIS.

NOTES ON THE COURSE AND SECONDARY SYMPTOMS OF CHLOROSIS.

BY CHARLES N. DOWD, M.D.,
ASSISTANT PHYSICIAN TO THE OUT-PATIENT DEPARTMENT OF ROOSEVELT HOSPITAL,
NEW YORK CITY.

IN the reports of five of the leading New York hospitals, for the year 1888, there were recorded 165 cases of "simple anæmia" in a total of 2250 female medical patients—that is, more than seven per cent. of all the female medical patients were cases of "simple anæmia." When we remember that more of these patients are treated in the out-patient departments than in the hospital wards, the disease seems still more common. In fact, we must consider it one of the most common of diseases.

The term "simple anæmia," as it is used in these reports, is usually synonymous with the term "chlorosis," as it is found in medical literature; we understand chlorosis to be a disease of young women[1] characterized by pallor, weakness, cardiac palpitation, "anæmic" cardiac murmurs, dyspnœa on exertion, disordered menstruation, fugitive pains, abnormal appetite, and constipation; these symptoms diminishing on the administration of iron, or of iron and laxatives.

Although the disease is so common, our knowledge of it is very indefinite. We know very little of its etiology. There is much dispute about the state of the blood, as to whether there is poverty in red corpuscles or only in hæmoglobin, as to the peculiarities of the blood-building under treatment, and as to what extent the condition of the blood may be used as a guide in diagnosis and treatment.

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[1] The few cases which are recorded in boys may be regarded as exceptions.

From a clinical standpoint we find the diagnosis often missed, secondary symptoms are mistaken for the main disease; or, on the other hand, pale patients are treated for chlorosis when the pallor is due to something else.

From a therapeutic standpoint we find improvement general, but many failures to effect a cure.

Hoping to make a slight addition to our knowledge of the subject and to demonstrate the possibility and desirability of more general blood examination for clinical purposes, I wish to record the results of the study of thirty-one cases of chlorosis as they have been treated in Roosevelt Hospital, New York City. No cases are mentioned which did not have enough of the above-mentioned symptoms to place the diagnosis beyond doubt.

The blood examinations were made to show the number of red corpuscles per c.mm., and the percentage of hæmoglobin during the different stages of the disease; certain observations of the size and shape of red corpuscles and of the number of white corpuscles were also made. The corpuscle numeration was done with the hæmacytometer of Thoma-Zeiss. Five per cent. seems a fair allowance for errors; this is the allowance granted by Lyon and Thoma (1)[1]. Ten estimations of blood from the same person gave results well within this limit. Two hundred squares were counted for each estimation. The instrument used gave 5,200,000 corpuscles per c.mm. as the average of ten counts from blood of healthy men and boys. In order to eliminate any errors which might come from the different methods of different observers the estimations were all made by the writer.

The patients were generally given five-grain Blaud's pills (iij to vij t. i. d.) and oxygen inhalations (gallons x b. i. d.), with symptomatic treatment for constipation and other by-symptoms.

Changes in the Number of Red Corpuscles.—It is my purpose to consider, first, the number of corpuscles when the patients were admitted to the hospital, and the relation between this number and the condition of the patients; next, the changes under treatment and their relation to the patient's condition; and, finally, the number after treatment.

There are thirty-four series of red corpuscle estimations, as three of the thirty-one patients were treated for relapses.

On admission the number of red corpuscles varied between 5,100,000 and 1,800,000 per c.mm.; the distribution between these points was fairly regular, as may be seen in this table:

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[1] The small figures in parentheses refer to the bibliography.

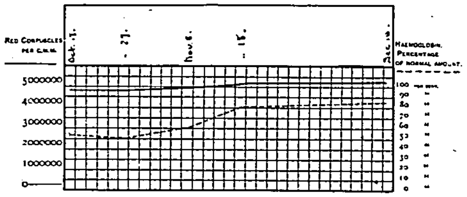
NUMBER OF RED CORPUSCLES ON ADMISSION.

5,100,000	per cubic millimetre,	1 patient.
4,500,000 to 5,000,000	" " "	4 patients.
4,000,000 " 4,500,000	" " "	7 "
3,500,000 " 4,000,000	" " "	5 "
3,000,000 " 3,500,000	" " "	5 "
2,500,000 " 3,000,000	" " "	6 "
2,000,000 " 2,500,000	" " "	5 "
1,800,000	" " "	1 patient.

Average 3,256,000

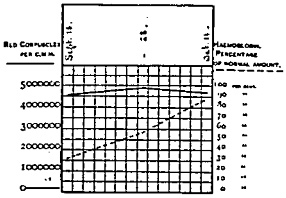
In a general way, the severity of the symptoms corresponded with the paucity in red corpuscles, but there were many exceptions to this. It is to be especially noticed that many of the patients who had a good number of corpuscles were suffering greatly from the disease—*e.g.*, cases 1, 2, 3, and 4, who had each more than 4,500,000, and Cases 5 and 6, and 7 on first admission, who had each more than 4,000,000; yet these seven

CHART 1.



Case 1. The continuous upper line indicates the number of red corpuscles, the broken lower line indicates the percentage of the normal amount of hæmoglobin.

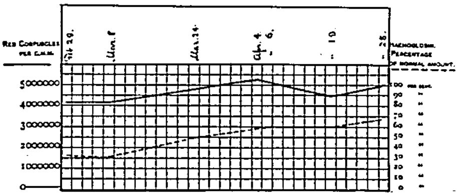
CHART 2.



Case 3.

cases were among the severer ones in the series; two of them could not walk more than a city block at an ordinary gait without very great exhaustion. Again, Case 8, on first admission, had 2,812,000; eleven months later she was treated for a relapse, and then had on admission 4,162,000. The difference in her symptoms on these two admissions did not at all correspond with this difference in the number of red corpuscles.

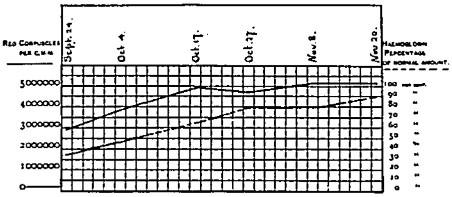
Chart 3.



Case 7. First admission.

A similar condition existed in Case 7, who, on first admission, had 4,204,000 red corpuscles per c.mm., and, on admission for a relapse seven months later, 2,932,000, and her symptoms were fully as bad on the first as on the second admission.

Chart 4.



Case 7. Second admission.

During the treatment there was an increase in the number of red corpuscles, but there were numerous variations and irregularities in this increase, ten cases at some stage of the treatment showing a diminution of 300,000 or more per c.mm.; this diminution was usually not from the number on admission but from the number attained at some time while under observation.

RECORD OF BLOOD EXAMINATIONS.

	Red corpuscles per c. mm.	Hæmoglobin, percentage of normal amount.	
Case 1 (see chart).			
Case 2	4,684,000	*45 per cent.	May 3.
	4,626,000	*56 "	May 18.
	4,328,000	*55 "	May 29.
	5,078,000	*70 "	June 6.
Case 3 (see chart).			
Case 4	4,660,000	. . . . .	March 29.
	4,900,000	. . . . .	April 5.
	5,200,000	. . . . .	April 14.
	*5,650,000	. . . . .	April 19.
Case 5	4,350,000	45 per cent.	June 20.
	4,800,000	70 "	June 29.
	4,800,000	95 "	July 14.
Case 6	4,422,000	65 "	Nov. 3.
	*3,988,000	65 "	Nov. 14.
	4,796,000	65 "	Nov. 26.
	4,464,000	75 "	Dec. 22.
Case 7 (see chart).			
Case 8 (first admission) .	2,812,000	30 per cent.	Nov. 22.
	3,054,000	40 "	Dec. 6.
	3,660,000	50 "	Dec. 11.
	4,876,000	60 "	Dec. 27.
	4,798,000	70 "	Jan. 4.
Case 8 (second admission)	4,162,000	50 "	Oct. 17.
	4,476,000	*55 "	Oct. 27.
	4,622,000	68 "	Nov. 8.
	4.984,000	80 "	Nov. 20.
Case 9 (see chart).			
Case 10 (see chart).			
Case 11	2.542,000	25 per cent.	Jan. 30.
	3,452,000	*45 "	Feb. 15.
	4,990,000	*85 "	March 7.
	3,982,000	75 "	March 19.
Case 12 (first admission) .	1,976,000	. . . . .	March 7.
	2,196,000	. . . . .	March 8.
	2,400,000	. . . . .	March 16.
	4,400,000	. . . . .	March 29.
Case 12 (second admission)	2,184,000	18 per cent.	Aug. 15.
	2,086,000	*18 "	Aug. 21.
	4,080,000	45 "	Sept. 8.
	4,650,000	75 "	Sept. 22.
	4,324,000	62 "	Oct. 4.
	4,086,000	68 "	Oct. 17.
Case 13 (see chart).			
Case 14	4,308,000	50 per cent.	Dec. 14.
	5,106,000	*45 "	Dec. 23.
	. . . . . .	*38 "	Jan. 6.
	. . . . . .	*55 "	Jan. 16.
	4,706.000	*80 "	Jan. 30.
Case 15	5,026,000	*60 "	March 12.
	. . . . . .	65 "	March 27.
	4,206,000	*85 "	April 6.
	4,598,000	*62 "	April 16.
	4,926,000	*65 "	April 30.
Case 16	3,274,000	40 "	Nov. 16.
	3,066,000	50 "	Nov. 26.
	3,946,000	75 "	Dec. 10.
	4,798,000	80 "	Dec. 22.
	4,540,000	75 "	Jan. 5.

* Verified by a second examination.

	Red corpuscles. per c. mm.	Hæmoglobin, percentage of normal amount.	
Case 17	2,456,000	*30 “	Feb. 20.
	4,380,000	*50 “	March 7.
	4,600,000	. . . . .	April 3.
	4,810,000	*65 per cent.	April 16.
	4,832,000	*65 “	May 3.
Case 18	2,574,000	20 “	Nov. 14.
	4,198,000	55 “	Nov. 30.
	4,674,000	60 “	Dec. 15.
Case 19	2,700,000	*23 “	Sept. 16.
	3,600,000	50 “	Sept. 26.
	3,722,000	*70 “	Oct. 6.
	4,228,000	75 “	Oct. 17.
	4,718,000	*75 “	Oct. 26.
	5,084,000	80 “	Nov. 4.
Case 20	4,050,000	43 “	Nov. 9.
	4,374,000	58 “	Nov. 20.
	4,592,000	*68 “	Nov. 30.
	4,888,000	75 “	Dec. 15.
Case 21	3,114,000	30 “	Nov. 16.
	2,902,000	35 “	Nov. 26.
	3,394,000	45 “	Dec. 6.
	3,960,000	60 “	Dec. 11.
Case 22	3,992,000	*37 “	June 25.
	3,996,000	*65 “	July 10.
	5,480,000	*75 “	July 20.
Case 23	2,332,000	34 “	Nov. 9.
	3,888,000	43 “	Nov. 20.
Case 24	3,342,000	31 “	Nov. 5.
	3,384,000	50 “	Nov. 17.
Case 25	4,104,000	55 “	Sept. 20.
	4,790,000	60 “	Sept. 29.
	. . . . . .	75 “	Oct. 11.
Case 26	3,072,000	45 “	Dec. 19.
	4,840,000	52 “	Dec. 30.
	4,750,000	50 “	Dec. 31.
Case 27	3,620,000	. . . . .	March 7.
	4,300,000	. . . . .	March 30.
	5,200,000	. . . . .	April 6.
Case 28	3,600,000	. . . . .	March 30.
	3,900,000	. . . . .	April 6.
	4,876,000	. . . . .	April 14.
Case 29	3,676,000	. . . . .	March 29.
	3,900,000	. . . . .	April 6.
	4,120,000	. . . . .	April 14.
	5,000,000	. . . . .	April 21.
	4,840,000	. . . . .	April 29.
Case 30	2,300,000	. . . . .	April 21.
	3,800,000	. . . . .	April 30.
	4,100,000	. . . . .	May 10.
	4,620,000	. . . . .	May 20.
Case 31	3,600,000	. . . . .	May 3.
	4,600,000	. . . . .	May 13.
	5,000,000	. . . . .	June 2.
	. . . . . .	*85 per cent.	June 8.
	5,100,000	. . . . .	June 14.
	5,400,000	90 per cent.	June 27.

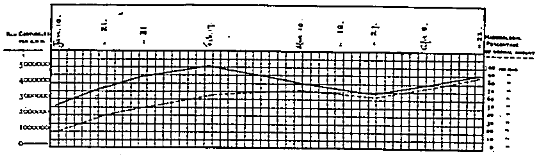
* Verified by a second examination.

DIMINUTION IN RED CORPUSCLES DURING TREATMENT.

Case 2,	4,684,000	to	4,328,000	per cubic millimetre.
" 6,	4,796,000	"	4,464,000	" " "
" 7,	5,324,000	"	4,350,000	" " "
" 9,	5,180,000	"	4,354,000	" " "
" 10,	5,064,000	"	3,428,000	" " "
" 11,	4,990,000	"	3,982,000	" " "
" 12,	4,650,000	"	4,086,000	" " "
" 13,	2,662,000	"	2,354,000	" " "
" 14,	5,106,000	"	4,706,000	" " "
" 15,	5,026,000	"	4,206,000	" " "

These variations are best shown in the charts and tables of blood estimations. Except in Cases 10, 11, and 12, the symptoms did not correspond with them, and in 10 and 11 the change in symptoms was not proportionate to that in corpuscles. The fallacy of judging the condition of the patient from the number of corpuscles would have been great; for instance, Cases 1, 2, and 3 would have been declared free from anæmia if the blood test had consisted simply of a corpuscle enumeration, yet these three cases averaged only 41 per cent. of the normal amount of hæmoglobin and were suffering greatly from anæmia. Again, Case 10 would have been pronounced better February 17th than April 23d, yet she had 23 per cent. more hæmoglobin April 23d, and was much stronger and better. From these considerations we can endorse Hayem's (2) statement that "the red corpuscles are a very changeable element of the blood." The simple estimation of their number is certainly of very little clinical value in chlorosis. On discharge from the hospital the condition was as follows:

CHART 5.



Case 10.

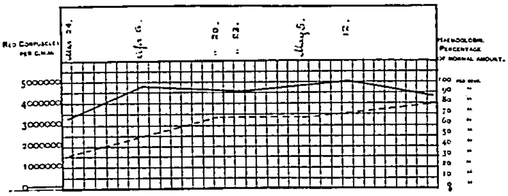
NUMBER OF RED CORPUSCLES ON DISCHARGE.

More than 5,000,000	. . . .	per cubic millimetre,	8	patients.
4,500,000	to 5,000,000	" " "	17	"
4,000,000	" 4,500,000	" " "	4	"
3,500,000	" 4,000,000	" " "	4	"
3,400,000	"	" " "	1	patient.

Average 4,704,000

It thus appears that it is usually easy to bring the number of red corpuscles above 4,500,000 per c.mm. The five cases who had less than 4,000,000 on discharge, left the hospital before treatment was completed. Of the four who had between 4,000,000 and 4,500,000, one was pregnant and one left before treatment was completed; but there were two (Cases 9 and 6) who were treated respectively nine and seven weeks, they had a diminution in the number of corpuscles before discharge.

Chart 6.



Case 9.

Change in Shape and Size of Red Corpuscles.—Blood from seven patients who were notably anæmic was drawn into a one per cent. watery solution of osmic acid; it showed large, small and irregular-shaped red corpuscles, the average diameter appearing less than normal.

The number of white corpuscles was estimated in twelve patients. The ratio was one white to about four hundred red.

Changes in the Hæmoglobin.—The hæmoglobin estimations were made with the Fleischl hæmometer. The results are given in percentages of the normal amount of hæmoglobin—*i.e.*, 100 per cent. indicates the normal, 50 per cent. one-half the normal amount. Numerous estimations of the blood of healthy persons have convinced me that the standard of the instrument used is correct. The results of two series of ten consecutive examinations of the blood of one person correspond within 4 per cent.

With this instrument I made twenty-eight series of hæmoglobin estimations. The results were much more uniform and much more satisfactory than in the enumeration of the blood corpuscles; the severity of the symptoms was found to correspond pretty closely with the poverty in hæmoglobin; hence, as a guide to the condition of the patient, the estimation of the hæmoglobin is much more valuable than the enumeration of the blood corpuscles.

An initial poverty in hæmoglobin was universal; so was an increase under treatment, and this increase was fairly regular, showing less variation than in the corpuscles.

This table shows the

PERCENTAGE OF HÆMOGLOBIN ON ADMISSION AND ON DISCHARGE:

	Admission.	Discharge.
91 per cent. to 100 per cent. . .	0	1
81 " " 90 " . .	0	5
71 " " 80 " . .	0	11
61 " " 70 " . .	2	5
51 " " 60 " . .	3	4
41 " " 50 " . .	5	2
31 " " 40 " . .	9	0
21 " " 30 " . .	5	0
15 " " 20 " . .	3	0
	Average 37⅓ per cent.	Average 72½ per cent.

It is noticeable that the percentage on admission was very low; more than one-half the cases had less than 40 per cent., three cases less than 20 per cent. of the normal amount, a diminution in hæmoglobin as great as that usually found in pernicious anæmia.

It is also noticeable that the hæmoglobin rarely reached the normal; only 6 of the cases registered above 80 per cent. when discharged. The 6 patients who registered below 61 per cent. left the hospital before treatment was completed; the same is true of 9 of the 16 who were between 60 per cent. and 81 per cent., the tenth was pregnant, the eleventh had a complicating nephritis which delayed convalescence, and the twelfth had a thrombosis of the internal saphenous vein, but there were 4 who were treated 7 weeks or more with no apparent cause for the failure to bring the hæmoglobin percentage higher, viz., Cases 12, nine weeks, and Cases 6, 11, and 15, each seven weeks. A similar condition was reported by Gräber (3) in 28 cases of chlorosis. The hæmoglobin did not reach the normal under treatment.

It is to be further noticed that the poverty in hæmoglobin always exceeded that in red corpuscles. This has often been stated as a constant condition in chlorosis; it certainly sometimes occurs in other diseases—*e. g.*, chronic phthisis and chronic Bright's disease.

In these cases the amount of hæmoglobin has been by far the best single guide there was to the patient's condition; whenever there has been a marked disparity between hæmoglobin and corpuscles the symptoms corresponded with the hæmoglobin, not with the corpuscles; in fact, the number of corpuscles gave a very poor guide to the patient's condition, and the percentage of hæmoglobin a very good one.

This is very important; the hæmoglobin estimation is an easy one; the corpuscle estimation is a tedious one. It takes three-quarters of an hour to make a careful corpuscle estimation, and one would hardly be willing to depend on a single count unless he had had considerable experience in the use of the instrument; moreover, a microscope must be used, and this is often a great inconvenience. These difficulties are so great that the number of corpuscles is not likely to be estimated extensively in clinical work.

On the other hand, the hæmoglobin estimation can be made in five to ten minutes, and duplicated in another five minutes, if desired; the instrument is small and easily carried, the technique is simple, no microscope is needed.

I see no reason why the hæmometer should not be one of the ordinary diagnostic instruments used by general practitioners.

There is good authority for the belief that the hæmoglobin estimation gives a good indication of the real condition of the blood.

Barbacci (4) estimated the hæmoglobin, but not the corpuscles, in twenty-eight cases of chlorosis, and concludes that the percentage of hæmoglobin indicates the real amount of the disease.

Hayem (2) states that the determination of the coloring power alone gives the exact measure of the degree of anæmia if the volume of the blood is normal.

Henry (5): "The principal point to be determined in an estimation of the blood is the functional value of the red corpuscles, which bears a direct ratio to the amount of hæmoglobin in each."

Jaccoud (6): "The fundamental lesion is the diminution in hæmoglobin, not the diminution in the number of red corpuscles."

We may thus feel that in the amount of hæmoglobin we have a good guide for our diagnosis and treatment, a guide which is reliable and which is now so easily accessible that it can be used in general practice. This certainly marks a step of advancement in this subject.

Oppenheimer (7) and Gräber (3) announce that they consider a normal number of red corpuscles and a diminution in hæmoglobin the characteristic blood condition in chlorosis. This varies so much from the generally accepted reports that it may be considered somewhat in detail.

Duncan (8), in 1867, reported the corpuscle number normal and the hæmoglobin diminished in 3 cases of chlorosis, but later observers consider that there may or may not be a reduction in red corpuscles, mild cases often showing no marked reduction. Oppenheimer's cases accorded with this in that they were mostly mild. Many of Gräber's cases must also have been mild, as the hæmoglobin averaged 52 per cent. In any event, positive evidence over-weighs negative, and numerous observers have found a diminution in corpuscles.

Quincke (9) states that there must be two kinds of chlorosis—one with a diminution in both hæmoglobin and corpuscles, and one with a diminution in hæmoglobin and a normal number of corpuscles. Henry (5): "In severe cases (of chlorosis) the number of corpuscles and the percentage of hæmoglobin are both reduced."

Flint (10) states that there may, or may not, be a reduction in the number of red corpuscles, but that there usually is. Gowers (17), Henry (5), Baxter and Wilcox (12), record 7 cases with an average corpuscle count of 3,250,000. Laache, Hayem, and Coupland are quoted (5) (18) as recording 38 cases, with an average corpuscle count of 3,450,000. Jaksch (14), Hartshorne (15), Weiss (16), Immerman (19), all state that the corpuscles are sometimes diminished. Again, Oppenheimer considers the number of corpuscles normal in those cases who have 4,000,000 per c.mm. This is certainly much lower than most observers put it. Sörensen (20) found 4,820,000 (the average) in 14 healthy young women, 15 to 28 years of age. Henry (5) compares corpuscles in chlorosis with 5,000,000 as the normal. Gowers (17) gives 5,000,000 as an average; Vierordt (21), 4,500,000 for women. In the cases which I record there was regularly an increase under treatment, even when there were more than 4,000,000 per c.mm. Therefore, on the basis of the results of other observers, there was really a diminution in red corpuscles in most of Oppenheimer's cases.

We feel confident that a normal number of corpuscles is not characteristic of chlorosis, but that such a discussion could have arisen at this time emphasizes the fact that corpuscle enumeration gives an uncertain guide; it throws us more and more onto the hæmoglobin estimation, and the value of the hæmoglobin estimation is the point which we wish especially to bring forward. The more hæmoglobin estimations are recorded the stronger is the evidence of their value. The more corpuscle enumerations are recorded the stronger is the evidence of their irregularity.

The results of the blood examinations may be summarized as follows:

1. There was usually an initial paucity of red corpuscles.
2. Under treatment it was easy to bring the red corpuscles to 4,500,000 per c.mm., and frequently higher.
3. The severity of the symptoms did not regularly correspond with the paucity of red corpuscles.
4. In the severer grades microcytes, megalocytes, and poikilocytes were found, the average diameter of the corpuscles being below the normal.
5. The reduction in hæmoglobin always exceeded that in red corpuscles and occasionally there was great poverty in hæmoglobin and very little in corpuscles.
6. The amount of hæmoglobin was a far better guide to the severity of the disease than the number of red corpuscles; it is so good a guide in chlorosis as to be sufficient in blood examination for ordinary clinical purposes.
7. The hæmoglobin increased regularly under treatment, but it was difficult to bring it above 85 per cent. of the normal.
8. No change was noticed in the white corpuscles.

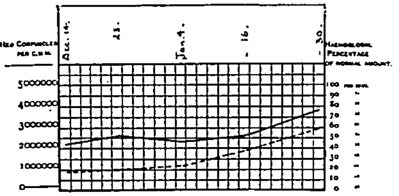
These results do not teach us the primary cause of chlorosis; but we do not yet know the cause of many diseases, nephritis or pleurisy with effusion, for instance, although we do know something about the pathological conditions when these diseases are established, and are guided in our treatment by this knowledge. Now regarding the blood as a tissue with cells and a fluid intercellular substance (Virchow (22), Prudden (23), Foster (24)), we are in the same relation to chlorosis that we are to the other diseases; we do not know the cause, but we do know the condition of the blood—at least we can know it as well as we do that of the kidneys and pleura in nephritis and pleurisy, and we should examine the blood in suspected cases as regularly as we examine the chest and urine of patients suspected of having the other diseases.

It is only by continuous observations and records that a groundwork has been gained for further advances in medical science; we now have a knowledge of the state of certain elements in the blood which furnishes a fair guide in diagnosis and treatment, general blood examinations are possible and we have a better groundwork for solving other problems in relation to chlorosis.

The question of treatment in chlorosis is still an open one. The improvement which regularly follows the administration of iron has led to its use almost as a specific, but the Roosevelt Hospital reports show a large proportion of failures to produce a complete and permanent cure.

In these cases the aim was to make a comparative study of the course of the blood-changes; therefore, the treatment was kept as nearly uniform as possible: Five-grain Blaud pills, iij to vij t. i. d. Oxygen inhalations, gallons x b. i. d. Still there were some variations from this treatment which affected the blood-changes.

CHART 7.



Case 13.

Case 13 received December 14th to January 4th sodii bicarb. gr. x and hydrarg. chlorid. corrosiv. gr. $\frac{1}{8}$ t. i. d. and inhalations of oxygen x gallons b. i. d., but no iron, and during this time there was hardly any change in the blood.

Case 14 received hydrarg. chlorid. corrosiv. gr. $\frac{1}{16}$ and potas. iodid. gr. x t. i. d. from December 14th to January 6th, and inhalations of oxygen x gallons b. i. d. from December 19th to January 6th. During this time her blood deteriorated.

Case 12 on second admission was given manganese binoxide, gr. ij to iv t. i. d., August 15th to 21st, with no improvement in the blood.

All these cases showed rapid improvement when given Blaud's pills and oxygen.

Case 8 on first admission did not do well on ordinary treatment, but improved rapidly on a laxative iron mixture. On returning with a relapse she was kept on laxatives alone for ten days, following the theory of Sir Andrew Clark (25) and M. Duclos (26), that chlorosis is the result of feculent retention and decomposition in the intestines. During these ten days the improvement was very slight, but it became rapid on the addition of iron and oxygen.

Case 10 (see chart) showed a remarkable improvement on rhubarb, soda, mint, and ipecac:

℞.—Rhei pulv.	gr. j.
Sodii bicarb.	gr. v.
Ipecac pulv.	gr. $\frac{1}{8}$.
Olei menth. piperit.	gr. $\frac{1}{20}$.

Make 1 tablet. Sig.—1 four times daily.

She had been treated two and one-half months on Blaud's pills and oxygen, and during the last month the blood had deteriorated and the chlorotic symptoms had increased. The above prescription was then substituted for the iron and oxygen and there was a steady improvement.

Case 3 had no oxygen and did well.

Case 9 had no oxygen for twenty-nine days and did well.

Case 15 had no oxygen and did not do well.

These observations confirm the value of Blaud's pills, but their value is so well established that there is no need for further proof. The point which is of most importance is that so many of the cases cannot be carried to complete recovery and so many have relapses. Improvement is general, complete recovery is rare. Few of the cases had normal blood when discharged, and at least seven of the thirty-one patients had relapses. Nos. 7, 8, and 12 had relapses which are recorded above. No. 7 has had a second relapse since. Nos. 6 and 23 have each had two similar previous attacks within four years, each lasting many weeks.

Case 10 has been treated four times for chlorosis in Roosevelt Hospital: August, 1885, to October, 1885; December, 1885, to January, 1886; November, 1886, to December, 1886; January, 1888, to April, 1888.

Case 24 had a decided attack eight years previously, and in the meantime had continually suffered from chlorotic symptoms.

Some of these cases were taking iron much of the time between relapses. Numerous similar cases are recorded: (27), (28), (29).

It is in these cases that the disease assumes its most serious aspect. If a young girl has an attack of chlorosis which lasts two or three months and ends in complete recovery, it is not a serious matter. She may have to stop school for a time and her friends may become anxious, but such an attack has no permanent bad effect. On the other hand, when the symptoms continue for years the results are very serious. The patient becomes a semi-invalid, all employment which requires ordinary health or strength has to be given up, attacks of gastric disturbance or headache, or pain, or palpitation, or vertigo, follow each other, and then hysterical symptoms arise which complete the ruin of a useful member of society.

I was consulted recently by a patient whose relatives were suspicious of a cancer of the tongue. The tongue was simply irritated by decaying teeth. She said she was unable to sit in a dentist's chair long enough to have the teeth filled, and the idea of having them extracted was quite unbearable. She always carried a bottle of valerian with her, and could not so much as make a call without using it. She was pale and weak and subject to attacks of palpitation and dyspnœa and indigestion. At the age of twenty-five she was a wreck, nervously and physically. Her history was as follows: Eight years ago she had a perfectly straightforward attack of chlorosis. She had recovered from the acute symptoms, but had gone on with the subacute ones until she reached the stage depicted. She had taken iron in various forms, but had always been weak, pale, and miserable, and had grown more and more nervous and hysterical. When seen she had 70 per cent. the normal amount of hæmoglobin. If the original chlorosis could have been treated successfully, and if the tendencies to relapse could have been controlled, she need not have fallen into her present condition, but it is in just these cases that our treatment is defective. We certainly are in great need of further studies as to the best method of treating these long-continuing cases. There is no lack of remedies which are recommended. Arsenic (32,6), albuminate of iron (39), hydrochloric acid after iron (40), alkalies and mild tonics (22), aloes (32), laxatives (25,26), sulphur (41), phosphorus (18), large doses of iron as opposed to small ones (42), and oxygen inhalations are among them. We have tried many of them without reaching the desired result. There is no doubt that a skilful selection from these remedies together with good hygienic surroundings would save many cases, but the fact still remains that many are not treated successfully. It would be interesting to know whether there is any direct relationship between these prolonged attacks and pernicious anæmia.

There are certain considerations in the etiology and symptoms of the disease which bear on the diagnosis. The age of the patient, the color of the face, pain, severe cardiac or digestive symptoms may any of them obscure the diagnosis. The facts which seemed of especial importance may be grouped as follows:

Occupation.—All did housework, or were shop or factory girls.

Age.—

16 years,	2 patients.	22 years,	5 patients.
17 "	5 "	23 "	3 "
18 "	2 "	24 "	1 patient.
19 "	4 "	25 "	1 "
20 "	4 "	26 "	1 "
21 "	3 "		

Fourteen—nearly one-half—were 21 or older. This is significant, as chlorosis is sometimes called a disease of puberty (5). However, Gowers (17), Gibson (30), and Jaccoud (6) record cases aged respectively 34, 30, and 25 years; Sörensen records cases from 17 to 34 years. Many of the older patients had some of the secondary symptoms prominent.

Nativity.—Irish, 24; French, 1; Welsh, 1; Swedish, 1; American, of foreign parentage, 4. Eleven had been in this country two years or less.

The only etiological factors which seem of importance in these statistics are that the average age was high and that many of the patients had not long been in America.

Family Histories.—Negative, excepting that in five cases a parent had died of phthisis.

Personal Histories.—No previous history of venereal, cardiac, renal, or serious pulmonary disease; no recent malarial symptoms; two cases had had slight attacks of rheumatism.

Nutrition.—All well nourished.

Color.—All pale when admitted; fifteen had a chalky white hue; under treatment a flush soon came to the face which was very deceptive; a chlorotic girl with one-half the normal amount of hæmoglobin might look ruddy while a phthisical patient with the same amount would look very pale. As the color is apt to be the first guide in diagnosis this peculiarity is important. Oppenheimer (7) has especially called attention to the fact that a pale color is no fair indication of the state of the blood, pale patients often having normal blood, but the converse is also true. Many patients with a flush on the face, or even a good color, have blood much impoverished; hence the importance of blood examinations in all doubtful cases is very evident.

Dyspnœa and palpitation of the heart on exertion were present in all cases.

Weakness was a very prominent symptom; nine of the patients could not walk a city block without much distress.

Attacks of vertigo were present in twenty-five cases.

Attacks of syncope were present in eight cases.

One case, 21, was brought into the hospital in an unconscious condition and remained so for two days; urine and feces were passed involuntarily; she had been incoherent for several days before admission; she had had no previous similar attacks and showed no tendency to a recurrence; there were no convulsions; she did well under iron and oxygen.

Another case, 24, was brought in suffering apparently from dementia; she had very marked symptoms of chlorosis; her mental condition improved rapidly when Blaud's pills and oxygen were administered.

In dispensary practice I have seen an anæmic patient show unmistakable signs of dementia, which disappeared when iron was administered.

Menstruation ceased in eleven cases, it was diminished in ten, irregular in three, irregular and diminished in three, and normal in four cases; a return under treatment was recorded in seven cases.

Ophthalmoscopic examinations were made in twenty-six cases and no retinal hemorrhages were seen.

Pain was a very common symptom, in four cases it was the symptom most complained of; headache was frequent in twenty-four cases; oppression in chest, cramps in legs and abdomen, epigastric, lumbar, iliac, and general shooting pains were continually recorded. In every case the pain disappeared when the anæmia was relieved, while treatment immediately against it was futile.

The digestive functions were very generally disturbed; twenty-six patients had poor appetites, fourteen of them had cravings for peculiar articles of diet, such as pickles, lemons, ice, chalk, etc.

Vomiting was common, very severe in eight cases—so severe as to be the main complaint. One of them had vomited blood and another "dark fluid." Here, again, we have a misleading symptom; the patients certainly had the symptoms of gastritis or of gastric ulcer; some of them had been treated for the gastritis, but without good result. However, in every case the gastric symptoms disappeared as the blood improved under the routine treatment.

When we hear of chlorotic patients being rigidly dieted, or having their stomachs washed out for their gastric disturbances or being blistered or cauterized for their pains, we feel that there is really much need for giving attention to these secondary symptoms and to the fact that they disappear when the anæmia is relieved.

The relation between constipation and chlorosis has recently been much considered, Sir Andrew Clark (25) claiming that "feculent retention is not only the rule but the characteristic sign" in chlorosis, and that the leucomaines and ptomaines produced in the intestine and absorbed are the real cause of the disorder; he quotes Bouchard as estimating that enough alkaloids are formed in the intestine in twenty-four hours to kill a man if absorbed.

M. Duclos (26) considers chlorosis eminently a result of auto-infection from decomposition of fecal matter in the intestine. However this may be, constipation was certainly the rule in these cases; twenty-two were constipated and the improvement was much retarded when the constipation was not relieved. In the one case (8) where laxatives were given for a time without iron there was little improvement. In another case (10, referred to above) laxatives and stomachics succeeded when iron had failed.

Physical Examination.—An anæmic heart murmur was present in all the cases but one (6); it was systolic, heard at the base, usually most distinct at the second left intercostal space. It was also heard at the apex in fourteen cases; transmitted to the left from the apex in eight cases. The apex murmur disappeared after treatment in all cases. The base murmur disappeared in all but seven; in these seven it was faint. They all left the hospital before complete recovery.

Cardiac dilatation in chlorosis has been often recorded. Stark (31), Duclos (26 *a*), Duckworth (32), Irvine (33), Forchheimer (34), and Jacoby (29), all report it.

I only attempted to record the position of the apex beat. In twenty-six cases it was in the fourth instead of the fifth space, the average distance from the median line being three inches. It was reported at various stages of the disease in twenty-two cases; in fifteen it was constant, in four it was slightly nearer the sternum on discharge than on admission, in three slightly nearer on admission than on discharge.

In eleven cases a continuous venous hum (bruit de diable) was heard in the vessels of the neck. It disappeared in all but two.

Physical examination of the lungs was negative in all cases.

The area of hepatic dulness was recorded in twenty-six cases; it was normal.

The area of splenic dulness was recorded in fourteen cases; it was slightly increased in one.

The temperature was frequently a little above the normal. The average oral temperature for all the cases on admission was 99.3° F. There was generally an afternoon rise of a fraction of a degree. There was a marked tendency to exacerbation under each slight provocation.

Urine.—Eight cases showed a trace of albumin, which disappeared; in other respects the urine was normal. The specific gravity averaged 1017. Jaccoud (6) records a case of temporary albuminuria; Molliere (13): thirty cases in whom the urea and urine were normal.

Œdema of the feet and legs was present in fourteen cases; of the face and eyelids in one case. It was temporary in every case.

Thrombosis of the internal saphenous vein was present in one case; recovery was apparently complete. I find cases of thrombosis in chlorosis reported by Rendu (35), Hanot and Mathieu (36), Jandot (37), and Tuckwell (38).

Epistaxis occurred in eight cases.

To review these clinical studies, we notice many points which bear on the diagnosis. Patients are often found over twenty years of age, and occasionally over twenty-five, who are manifestly suffering from chlorosis and who do not differ from the younger ones, excepting that the disease has usually been of longer standing, that it yields less readily to treatment, and that the secondary symptoms are especially prominent. The color of the face may be deceptive.

There are often secondary symptoms which obscure the diagnosis. Pain, vomiting, vertigo, even unconsciousness for several hours, mental disturbance, amenorrhœa, palpitation, œdema, temporary albuminuria, thrombosis, are all capable of doing so.

Among these cases the pain has led to the diagnosis of rheumatism and "neuralgia;" the vomiting and other gastric disturbance, to that of gastritis or possible gastric ulcers; the mental disturbance, to that of dementia; the palpitation and cardiac murmurs, to that of endocarditis; the œdema and albuminuria, to nephritis. Yet these symptoms all disappeared under treatment for chlorosis and they all are common in chlorosis.

The diagnosis of a straightforward case of chlorosis is simple. It is often difficult when there are marked secondary symptoms, and the effects of a wrong diagnosis are serious. If a patient who simply needs Blaud's pills is told she has Bright's disease and treated for the same, she and her friends are made miserable, and instead of being benefited she is injured. If she is burned, or blistered, or dieted, or has her stomach washed out, she suffers at the hands of her physician as truly as does a patient at the hands of a surgeon when she endures an unnecessary operation.

Furthermore, judging from observations not recorded here, we believe that there are hundreds of cases where a moderate amount of chlorosis is an accompaniment of another condition and where the successful treatment of the other condition is much easier when iron is administered for the chlorosis.

As regards the course and treatment of the disease, it must be noted that relapses are frequent and that it is difficult to bring about a complete cure, many cases running on for months or years, suffering more or less from the symptoms of chlorosis.

Whether these cases are allied to pernicious anæmia or not we do not know, but we do know that we have here a disease which is chronic in its course, severe in its symptoms, and difficult of treatment, and that we need more studies both about its pathology and its treatment.

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